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## ORIGINAL ARTICLES

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## Exertional Heatstroke in an Infantry Soldier Taking Ephedra-Containing Dietary Supplements

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This is a case report of a highly trained, heat-acclimatized infantry soldier who suffered from exertional heatstroke during a 12-mile road march shortly after taking an ephedra-based supplement. Heatstroke is associated with systemic complications and a high mortality rate if not recognized early. Control of risk factors is key to the prevention of heatstroke. Since there are no clear ergogenic benefits in using ephedra alone, clinicians and military commanders should strongly discourage the use of ephedra-containing substances in active duty soldiers undergoing strenuous exercise.

### Introduction

Exertional heatstroke has been described in the athletic and military populations and is usually associated with strenuous exercise in hot environments.<sup>1</sup> Other risk factors include poor heat acclimatization, previous heat injury, underlying medical illness, and certain medications.<sup>1</sup> The use of ephedra alkaloids has previously been associated with myocardial infarction, strokes, seizures, and sudden death.<sup>2-4</sup> However, the use of ephedra-containing substances has not been previously described in a case of exertional heatstroke.

### Case Report

A 20-year-old active duty infantry soldier presented to the troop medical clinic with exertional collapse, mental status changes, and core body temperature of 106°F. He was near the end of a 12-mile road march conducted with an approximately 35-lb backpack load when he suddenly collapsed 0.5 mile from the finish line. The ambient temperature at the time of collapse was 66°F. He was brought to the clinic where he was found to be alert but not oriented to person, place, or

time. Initial vital signs found a blood pressure of 140/90, pulse of 118 beats per minute, and rectal temperature of 106°F. His skin was warm, flushed, and sweaty. After removal of all clothing, immediate ice packing and evaporative cooling techniques were undertaken. With lowering of rectal temperature to 102°F, mental status normalized. After stabilization of temperature and initiation of an intravenous line, he was given 1 L of normal saline and was transferred to a local hospital. Initial laboratory results were significant for a creatine kinase of 1,388 U/L, blood urea nitrogen of 24 mg/dL, creatinine of 1.9 mg/dL, aspartate aminotransferase of 46 U/L (5-40), and phosphate of 1.2 mg/dL (2.5-4.5). There was no evidence of coagulopathy. Twelve hours after admission, his creatine kinase peaked at 16,115 U/L. Intravenous fluids were initiated to maintain adequate urinary output, and his creatine kinase continued to trend downward until discharge. He did not have any further complications and was discharged on hospital day 5.

Upon further questioning, the patient reported that he had ingested two capsules of Xenedrine RFA-1 the night before the road march and two capsules immediately before the start of the road march event. According to the package label,<sup>5</sup> ([http://www.cytodyne.com/products/xenedrine/supp\\_facts.asp](http://www.cytodyne.com/products/xenedrine/supp_facts.asp)) each capsule contained ma huang (10 mg of ephedrine), bitter orange (2.5 mg of synephrine), and guarana extract (100 mg of caffeine). He denies taking any other medications or supplements. He also states that during the event, he drank over 3 L of water from a backpack reservoir and additional water sources in the approximate 3 hours of strenuous exercise before his collapse. Additional questioning regarding his training revealed adequate heat acclimatization. One month prior to this event, he had completed similar training road marches of 8, 8, and 10 miles in warmer weather without any complications. He denied any previous use of ephedra-containing supplements or any previous heat injuries.

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## Discussion

Exertional heatstroke presents commonly with high core body temperature ( $>40^{\circ}\text{C}$ ) and central nervous system dysfunction often associated with strenuous exercise in the heat.<sup>8,7</sup> Many medications and drugs, including neuroleptics, anticholinergics, alcohol, and amphetamines have been implicated as a risk factor for heatstroke.<sup>18-19</sup> Although ephedra is theoretically thought to predispose an individual to heat-related injuries,<sup>11</sup> this is the first known case report of exertional heatstroke associated with its use. Other risk factors associated with heatstroke include cardiovascular disease and underlying medical conditions, poor acclimatization, salt or water depletion, excessive ambient temperature, and lack of physical conditioning.<sup>1,8-10</sup> However, this highly trained infantry soldier was physically fit, adequately acclimatized in the heat, and was not overly hypovolemic. He also had recently completed several train-up road marches in warmer weather without any previous heat-related injury.

Ephedra alkaloids have previously been implicated in numerous adverse cardiovascular and central nervous system events to include: myocardial infarction, stroke, seizure, and sudden death.<sup>2-4</sup> The Food and Drug Administration has received more than 600 adverse event reports and is considering withdrawing it from the U.S. market (<http://www.fda.gov/OHRMS/DOCKETS/98fr/D40300c.txx>,<sup>12</sup> <http://vm.cfsan.fda.gov/~lrd/lr00049a.html>).<sup>12</sup> A recent study has implicated the increase in heatstroke fatalities in American football athletes from 1995 to 2001 to the increased use of dietary supplements containing ephedra and creatine resulting from the 1994 Dietary Supplements Health and Education Act.<sup>11</sup> This law led to the explosion of available health supplements, such as ephedra, without Food and Drug Administration regulation. Although the mechanism of heatstroke and injury is not entirely clear, ephedra may produce a thermogenic effect by activation of dopamine receptors and by impairing heat dissipation through peripheral vasoconstriction.<sup>14-16</sup> Also, hyperthermia is frequently seen with an overdose of amphetamines,<sup>14</sup> which is molecularly similar to ephedrine.<sup>17</sup>

As with all case reports, a clear causative mechanism cannot be concluded. However, in this highly trained, heat-acclimatized infantry soldier, ephedra alkaloids may have contributed to his exertional collapse and eventual heatstroke. A recent survey suggests that approximately 60% of Army soldiers use nutritional supplements containing ephedra or other substances.<sup>18</sup> Furthermore, studies do not show any clear ergogenic properties of ephedra alone.<sup>19</sup> Until the Food and Drug Administration makes a decision to remove ephedra from the U.S. market, the risk of life-threatening injury may outweigh any real or per-

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ceived benefit of ephedra and clinicians and commanders should strongly discourage its use in active duty soldiers.

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